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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09 166,649	10 05 1998	ANN MARIE SCHMIDT	56613 JPW JM	9377

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EXAMINER

O HARA, EILEEN B

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 12.19.2001

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/166,649

Applicant(s)

SCHMIDT ET AL.

Examiner

Eileen B. O'Hara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-8,11-13,15,17,18,20-22 and 24-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-8,11-13,15,17,18,20-22 and 24-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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DETAILED ACTION

1. Claims 1, 2, 4-8, 11-13, 15, 17, 18, 20-22 and 24-29 are pending in the instant application. Claim 11 has been amended and claims 3, 9, 10, 14, 16, 19, 23 and 30-57 have been canceled as requested by Applicant in Paper Number 12, filed Oct. 10, 2001.

All claims are currently under examination.

Withdrawn Objections

- 2.1 The objection to the specification is withdrawn in view of Applicants' amendment.
- 2.2 The objection to the claims is withdrawn in view of Applicants' amendment.

Withdrawn Rejections

- 3. The rejection of claims under 112 § 1 is withdrawn in view of Applicants' amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

- 4.1 The rejection of claims 11 and 12 are maintained under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) in a competitive assay using a peptide that is a carboxyl-lysine-modified AGE, does not reasonably provide enablement for a peptide derivative comprising an alkyl group. The specification does not enable any person skilled in the art to which it pertains,

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or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The rejection is maintained for reasons of record in the previous Office Action, Paper No. 11, at pages 3-4.

Applicant traverses the rejection and asserts on page 6 of the amendment that "inactivation by derivitization" is described in applicants' specification at page 12, lines 21-31, specifically citing examples of such chemical modifications, including making an alkyl derivative, all of which would be known to one of skill in the art. Applicants contend that these comments obviate the above rejection.

Applicants' arguments have been considered but are not persuasive. Although these statements are present in the specification as indicated, the statements themselves are not enabling of the method. The specification teaches a number of experiments that were performed to elucidate the specific binding of AGE peptides to a RAGE, or the effects of these AGE peptides on various cell types (Figures 1-7 and pages 4-6 of the specification). However, the only AGEs that were used in these experiments were carboxyl-lysine (CML), pentosidine, and methylglyoxal modified proteins. In Figure 1 and in the Brief Description of the Drawings on page 4 and the results section on pages 33-34, it was demonstrated that in the radioligand binding assays in which CML-BSA, pentosidine-BSA or methylglyoxal-human serum albumin were tested, only CML-BSA specifically bound to RAGE. Both pentosidine-BSA and methylglyoxal-HSA did not bind specifically to RAGE. Similar results were found in the other experiments shown in Figures 2-7 and in the results section. There were no experiments performed with a peptide comprising an alkyl derivative. The prior art does not disclose that peptides comprising an alkyl derivative are AGEs, or that they would bind to RAGE.

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It is not disclosed and not predictable from the limited teachings of the prior art and specification that a peptide comprising an alkyl derivative would bind to a RAGE and function in a competitive binding assay, as claimed, and Applicants have not presented fact or evidence to overcome the rejection. There is no guidance in the specification that such compounds would bind to RAGE, and the specification has not disclosed a single working example showing that such derivatives would bind. It is not predictable, based on the information provided in the specification or from the prior art, that the claimed compositions could be used in such assays, especially in light of the experimental results that teach that only the carboxymethyl-lysine-modified peptide specifically bound to RAGE. The specification has not provided the person of ordinary skill in the art the guidance necessary to be able to use a peptide comprising an alkyl derivative in the assay as claimed. Therefore, the method of using such derivatives is not enabled, and the rejection under 35 U.S.C. 112 first paragraph is maintained.

4.2 The rejection of claim 29 is maintained under 35 U.S.C. 112, first paragraph, because the specification is not enabling of the method claimed, for reasons of record in the previous Office Action, Paper No. 11, at pages 4-5.

Applicant traverses the rejection and asserts on page 8 of the amendment that one skilled in the art of competition assays for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) would understand the specification on page 9, lines 34 and 35, "In another embodiment of the screening method, the admixing of step (a) occurs in a cell," to be sufficiently enabling to carry-out in vitro experiments when viewed in light of page 9, lines 20, i.e. "the screening method may be carried

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out in vitro,, or wherein the components in step are admixed inside of a cell.” Applicants contend that these comments obviate the above rejection.

Applicants’ arguments have been considered but are not persuasive. Although these statements are present in the specification as indicated, the statements themselves are not enabling of the method. The specification or the prior art has not provided the person of ordinary skill in the art the guidance necessary to be able to use the peptide comprising an alkyl derivative in the assay as claimed. An additional literature search by the Examiner failed to discover a single instance in which a competitive binding assay as described in claim 1 is performed inside a cell. Therefore, the rejection under 35 U.S.C. 112 first paragraph is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. Claims 1, 2, 5-8, 13, 15, 17, 18, 20-22 and 24-28 remain rejected under 35 U.S.C. 102(e) as being anticipated by Morser et al., PN 5,864,018, for reasons cited in the previous Office Actions, Paper Nos. 9 and 11.

Applicants’ traverse the rejection and maintain that Morser et al. does not disclose every

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limitation of applicants' claimed invention for reasons cited in the previous response to July 10, 2001 Office Action, at pages 11 and 12, and applicants contend that these comments obviate the above rejection.

Applicants' comment have been considered but are not persuasive. Applicants' arguments were addressed in the previous Office Action, Paper No. 11 at pages 6-7, and as no new arguments have been set forth, the reasons for the rejection are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claim 4 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Morser et al, as applied to claims 1, 2, 5-8, 13, 15, 17, 18, 20-22 and 24-28 and further in view of Reddy et al, for reasons cited in the previous Office Actions, Paper Nos. 9 and 11.

Applicants' traverse the rejection and assert that the mere fact that references can be combined does not make the resultant combination obvious unless the prior art also suggests the desirability of the combination. Applicants contend that the prior art does not suggest the desirability of the combination of Reddy et al. and Morser et al. when viewed well within the ordinary skill of the art at the time the claim was made. Therefore, applicants contend that the Examiner used impermissible hindsight when combining Morser et al. and Reddy et al. to demonstrate *prima facie* obviousness in claim 4. Applicants argue that while Reddy et al.

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teaches that carboxy-methyl-lysine-modified peptides are a dominant AGE, it would not have been *prima facie* obvious to one skilled in the art of AGE/RAGE art at the time of the invention to use a carboxymethyl-lysine-modified peptide of Reddy et al. as the AGE in the AGE/RAGE competition assay of Morser et al. Applicants further point out that Reddy et al. demonstrates antigenic dominance of the N^ε (Carboxymethyl) lysine form of AGE in tissue proteins, not the specificity of its binding to RAGE, and that Lander et al. and Yan et al. demonstrate a complex experimental landscape of heterogeneous AGE/RAGE interactions mediated by oxidant stress. Applicants assert that accordingly, combining knowledge of antigenic dominance of a particular peptide with knowledge of the state of the work within a field of complex heterogeneous AGEs does not necessarily enable one of ordinary skill in the art to determine AGE/RAGE binding efficiency. Applicants contend that these comments obviate the rejection.

Applicants' comment have been considered but are not persuasive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Since Reddy et al. demonstrated that carboxymethyl-lysine was a dominant form of AGE at the time of the invention, it would have been *prima facie* obvious for one of ordinary skill at that time of the invention to use modified carboxymethyl-lysine peptides in the AGE/RAGE assay,

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because an "AGE" is defined as a compound that binds to a receptor for an AGE. Therefore, the rejection under of 35 U.S.C. 103 is maintained.

It is believed that all pertinent arguments have been answered.

Conclusion

7. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242.

Informal papers filed by fax should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

A handwritten signature in cursive script, reading "Lorraine Spector". The signature is written in dark ink and is positioned to the right of the printed name.

LORRAINE SPECTOR
PRIMARY EXAMINER